

IN THE CLAIMS:

Amend the claims as follows.

1. (Original) A method for the diagnosis or prognosis of papilloma or for the determination of the risk to develop a papilloma, comprising the determination of the level and/or the activity of :

- (a) a transcription product of a gene coding for PED/PEA-15, and/or
- (b) a translation product of a gene coding for PED/PEA-15, and/or
- (c) a fragment or derivative of said transcription or translation product,

in a sample coming from a subject, to whom a papilloma is to be diagnosed or prognosticated, comparing said level and/or activity to a reference value representative of a papilloma or health status, then formulating a diagnosis or a prognosis of papilloma in said subject or determining if said subject is at risk of developing a papilloma.

2. (Original) A method for monitoring the progression of a papilloma in a subject, comprising the determination of the level and/or activity of :

- (a) a transcription product of a gene coding for PED/PEA-15, and/or
- (b) a translation product of a gene coding for PED/PEA-15, and/or
- (c) a fragment or derivative of said transcription or translation product,

in a sample coming from said subject and comparing said level and/or activity to a reference value representative of a papilloma or health status, then monitoring the progression of papilloma.

3. (Original) A method for the evaluation of a therapeutic treatment of a papilloma in a subject, comprising the determination of the level and/or activity of :

- (a) a transcription product of a gene coding for PED/PEA-15, and/or
- (b) a translation product of a gene coding for PED/PEA-15, and/or
- (c) a fragment or derivative of said transcription or translation product,

in a sample coming from said subject and comparing said level and/or activity to a reference value representative of a papilloma or health status, then evaluating the treatment of papilloma.

4. (Previously Presented) The method according to claim 1, wherein said sample is a skin sample.

5 (Previously Presented) The method according to claim 1, wherein said reference value is the value of the level and/or activity of :

- (a) a transcription product of a gene coding for PED/PEA-15, and/or
 - (b) a translation product of a gene coding for PED/PEA-15, and/or
 - (c) a fragment or derivative of said transcription or translation product,
- in a sample coming from a subject who is not affected by papilloma.

6. (Previously Presented) The method according to claim 1, wherein said transcription and/or translation product and/or fragment or derivative is, respectively, mRNA and/or the PED/PEA-15 protein and/or a fragment or a derivative thereof.

7. (Previously Presented) The method according to claim 1, wherein said transcription product and/or fragment or derivative is determined by means of PCR or Northern blot analysis.

8. (Previously Presented) The method according to claim 1, wherein said translation product and/or fragment or derivative is determined by means of an immune assay, an enzyme activity assay and/or a binding assay.

9. (Previously Presented) The method according to claim 1, further comprising the comparison with a level and/or activity of

(a) a transcription product of a gene coding for PED/PEA-15, and/or

(b) a translation product of a gene coding for PED/PEA-15, and/or

(c) a fragment or derivative of said transcription or translation product,

in a series of samples coming from said subject and collected in a period of time.

10. (Original) The method according to claim 9, wherein said subject receives a therapeutic treatment before the collection of one of the periods of time.

11. (Previously Presented) The method according to claim 9, wherein said level and/or activity is determined before and after the treatment of said subject.

12. (Original) A kit for the diagnosis or prognosis of papilloma or for the

determination of the risk of developing a papilloma or for the monitoring of the progression of a papilloma or for the evaluation of a therapeutic treatment of a papilloma comprising a transcription product of a gene coding for PED/PEA-15, and/or a translation product of a gene coding for PED/PEA-15, and/or a fragment or derivative of said transcription or translation product.

13. (Original) A non-human transgenic animal comprising a non-native genetic sequence coding for PED/PEA-15, or a fragment or a derivative thereof, its progeny and different transgenic lines.

14. (Original) The animal according to claim 13, expressing PED/PEA-15 ubiquitously.

15. (Original) The animal according to claim 13, expressing PED/PEA-15 specifically or preferentially in a particular tissue.

16. (Previously Presented) The animal according to claim 13, which is mammal.

17. (Original) The animal according to claim 16, which is a mouse.

18. (Previously Presented) The animal according to claim 13, wherein a disruption of said gene results in a predisposition to developing a papilloma.

19. (Previously Presented) A method for obtaining the animal of claim 13 comprising:

(a) providing a gene targeting construct comprising said gene sequence and a selectable marker sequence, and

(b) introducing said construct in a stem cell of a non-human animal, and

(c) introducing said stem cell in a non-human embryo, and

(d) transplanting said embryo in a non-human pseudopregnant animal,

and

(e) allowing said embryo to develop to term, and

(f) identifying a genetically altered non-human animal whose genome comprises a modification of said gene sequence in both alleles, and

(g) breeding said genetically altered animal to obtain a non-human animal whose genome comprises a modification of said endogenous gene.

20. (Original) An animal obtainable by the method of claim 19.

Claims 21-24. (Canceled)

25. (Original) An assay for the screening of a substance useful for the treatment of papilloma comprising:

(a) contacting a biological model of papilloma with said substance;

(b) measuring the activity and/or the level of a second substance selected in the group consisting in a transcription product of a gene coding for PED/PEA-15,

and/or a translation product of a gene coding for PED/PEA-15, and/or a fragment or derivative of said transcription or translation product,

(c) measuring the activity and/or the level of said second substance in a control biological sample, which was not contacted with said substance;

(d) comparing the activities and/or levels of steps (b) and (c) and determine whether said substance is a inhibitor of said second substance.

26. (Previously Presented) The assay according to claim 25, wherein said model of papilloma is the animal of claim 13, or any part of it.

27. (Previously Presented) A substance obtainable by the assay of 25 for the preparation of a medicament for the prevention and/or treatment of papilloma.

28. (Original) An antisense oligonucleotide targeted to nucleobase 1 to nucleobase 100 of a nucleic acid molecule encoding PED/PEA-15.

29. (Original) The antisense oligonucleotide according to claim 28, said oligonucleotide being targeted to sequences encompassing nucleobase 70, 71 or 72 of a nucleic acid molecule encoding PED/PEA-15.

30. (Previously Presented) The antisense oligonucleotide according to claim 28, wherein said oligonucleotide is 8 to 30 nucleobases in length.

31. (Original) The antisense oligonucleotide according to claim 28 selected from the group consisting of 5'-tgacgcctccggagctgaga-3' and 5'-tgacgcctctggagctgagc-3'.

32. (Previously Presented) The antisense oligonucleotide according to claim 28, wherein the modified internucleoside linkage is a phosphorothioate linkage and/or the antisense oligonucleotide comprises at least one modified sugar moiety and/or antisense oligonucleotide comprises at least one modified nucleobase.

33. (Original) The antisense oligonucleotide according to claim 32, wherein the modified sugar moiety is a 2'-o-methoxyethyl sugar moiety.

34. (Original) The antisense oligonucleotide according to claim 32, wherein the modified nucleobase is a 5-methylcytosine.

35. (Previously Presented) A method of preparing a medicament comprising formulating a oligonucleotide of claim 28 as a medicament.

Claims 36-39. (Canceled)

40. (Previously Presented) A pharmaceutical composition comprising at least a substance of claim 27 in admixture with at least a pharmaceutically acceptable vehicle or excipient.

41. (Original) The pharmaceutical composition according to claim 40, suitable for topical administration.

42. (Original) The pharmaceutical composition according to claim 40, further comprising at least an antitumor active ingredient.

43. (Original) The pharmaceutical composition according to claim 42, wherein said antitumor active ingredient is TRAIL.

Claim 44. Canceled